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The big mush

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The big mush: psychometric measures are confounded and non-independent in their association with age at initial diagnosis of Ischaemic Coronary Heart Disease

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The present study uses early diagnosis of ischaemic coronary heart disease (ICHHD) as a proxy for disease malignancy in testing the statistical strength of association, and uniqueness/confounding, of several psychometric scales that have previously been found to prospectively predict death in cardiac samples (Beck Depression Inventory, Crown-Crisp Phobic Anxiety Scale, Type D Scale & Ketterer Stress Symptom Frequency Checklist). Eighty-three patients (no. of females = 35) with documented ICHHD were assessed for traditional and psychometric risk factors. The psychometric risk factors were moderately to strongly intercorrelated, and strongly confounded in their relationship to age at initial diagnosis. In a stepwise multiple regression, only the AIAI (aggravation, irritation, anger and impatience) scale of the Ketterer Stress Symptom Frequency Checklist (KSSFC) survived as a predictor of age at initial diagnosis ($P = 0.016$). In a subgroup of the sample for whom the Spouse/Friend Version of the KSSFC was received ($n = 58$, or 70%), spouse/friend reported AIAI survived as the only predictor ($P = 0.010$). While present results need replication in a prospective study of diagnosed ICHHD patients for all important clinical outcomes, only one psychometric screening instrument may be necessary to identify patients in need of treatment. *J Cardiovasc Risk* 9: 41–48 © 2002 Lippincott Williams & Wilkins.

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Introduction

Standard cardiovascular risk factors can only account for about half of all cases of ischaemic heart disease in the United States [1–3]. Therefore identifying additional factors associated with the onset or aggravation of ischaemic coronary heart disease (ICHHD) remains a high priority task. It has been known since the birth of cardiology that acute emotional arousal influences acute cardiac function [4]. However, only in the last two to three decades has epidemiological evidence been amassed demonstrating that psychosocial/emotional distress is, in fact, a strong prospective predictor of clinical outcomes [5–20].

The mechanisms underlying this relationship are probably multiple [21–24], and involve both psychoneuroendocrine (for example, provocation of ischaemia or platelet aggregability/adherence by acute or chronic emotional arousal) and psychobehavioural (for example, decreased compliance such as diminished smoking cessation, or maintenance of abstinence) pathways. As the only true experiment in risk factor research, several randomly-assigned, controlled treatment studies targeting psychosocial/emotional distress, and finding improved chest pain [25–28] as well as decreased myocardial infarction or death [16,18,29], have made this area of research arguably one of the most promising venues for future therapeutic advances.

One major barrier to routine use of emotional distress as a clinical target for improving outcomes in ICHHD is the lack of a consensually accepted method for bedside or clinic identification of patients likely to benefit from treatment. Should all patients with ICHHD be referred to behavioural evaluation and intervention? Or is there an identifiable subset of patients who are likely to benefit? How can the non-behaviourally trained internist or cardiologist efficiently and effectively identify those patients with ICHHD who need further work-up and treatment? Available prospective studies suggest that brief psychometric screening may provide a means for identifying patients needing further

evaluation/treatment. However, because all previous prospective studies contain only one or a few psychometric measures, no single-sample comparison of the relative strength and independence of the available measures exists.

One empirically rational way of determining the most promising screening tools is to use the strongest published univariate risk ratios for mortality. While one could make a case for using only the residual risk ratio after the influence of other risk factors has been removed from the outcome variable, at least two obvious objections to this strategy exist. First, investigators have not always been exhaustive, thorough and consistent about including all the major cardiovascular risk factors in their studies. This lack of uniformity means that any test of residual risk compared across studies will likely be misleading. Secondly, a number of the major cardiovascular risk factors may in fact be mediating pathways for the impact of the psychosocial factor (for example, compliance with smoking cessation and/or relapse avoidance). To remove the influence of the mediating risk factor would incorrectly remove some of the relevance of the psychosocial factor. Thus, the most straightforward way of assessing the potential predictive power of the psychosocial risk factors is to use published unadjusted risk ratios. These risk ratios are noticeably larger than those observed for standard cardiovascular risk factors [1–3,18]. The most promising measures available in English are displayed here (Table 1) with their best reported unadjusted risk ratios for death in various ICHD populations.

These psychometric screening tools have all shown promise as prospective predictors of cardiac events, but

Table 1 The psychometric scales with the strongest published univariate risk ratios for death in cardiac populations

Psychometric Measure	Unadjusted	
	Risk Ratio	Reference
Barefoot Composite Index of the Cook–Medley Ho Scale	5.54	Barefoot <i>et al.</i> , 1989 [8]
Maastricht Questionnaire	1.39	Appels & Mulder, 1989 [7]
Crown–Crisp Phobic Anxiety Scale	3.77	Haines <i>et al.</i> , 1987 [13]
	3.74	Kawachi <i>et al.</i> , 1994 [69]
Cornell Medical Index Anxiety Scale	2.74	Kawachi <i>et al.</i> , 1994 [14]
MMPI Anger Scale	3.58	Kawachi <i>et al.</i> , 1996 [15]
Beck Depression Inventory	7.82	Frasure-Smith <i>et al.</i> 1995 [40]
	2.36	Carney <i>et al.</i> , 1988 [9]
Ketterer Stress Symptom Frequency Checklist–‘Denial’ of AIAI	4.41	Ketterer <i>et al.</i> , 1998 [17]
Type D Scale	3.8	Denollet & Brutsaert, 1998 [38]
	3.9	Denollet <i>et al.</i> , 1996 [11]
	6.4	Denollet <i>et al.</i> , 2000 [39]

the Crown–Crisp Phobic Anxiety Scale, Cook–Medley Ho Scale, Type D Scale, Ketterer Stress Symptom Frequency Checklist and Beck Depression Inventory have shown the strongest or most consistent capacity for predicting events.

It has long been suspected that cardiac patients are prone to ‘denying’ or minimizing the degree of their emotional distress [30–36]. Several empirical investigations now support this belief:

- (1) Expert-rated ‘potential for hostility’ predicts morbidity and mortality in initially healthy populations [10] as well as restenosis among patients referred for catheterization following angioplasty while self-report does not [37];
- (2) Social inhibition in combination with acknowledged emotional distress predicts mortality in patients with ICHD [11,38,39];
- (3) ‘Anger-in’ (the acknowledged propensity to suppress the experience/expression of anger) predicts arrhythmic events among ICHD patients [40];
- (4) ‘Defensive hostility’ (high social desirability in combination with cynical beliefs about others) predicts which ICHD patients become ischaemic with mental stress provocation [41];
- (5) Spouse, but *not* self-, ratings of hostile attributions predict the presence of reversible defects on thallium imaging [42];
- (6) On parallel versions of the same questionnaire, spouse or friend perceived depression correlates with coronary artery disease severity while self-reported depression does not [43]; and
- (7) Denial of anger (spouse/friend minus self-report) is a strong independent predictor of mortality in patients with ICHD [17].

Thus, while the psychological mechanism(s) causing this difficulty in relying on self-report are unclear, and perhaps not even consistent from person to person or, for a given individual, from time to time [44,45], its pertinence to quantifying psychosocial/emotional distress is becoming unavoidable. In clinical care, a long tradition of checking collateral sources (e.g., laboratory tests, exogenous stressors or reports from family, nursing staff, medical records) to confirm the presence or absence of stigmatized behaviours (e.g., alcohol/drug

use, psychiatric conditions) exists. We have developed an objective, healthy-population normed method of quantifying 'denial' of emotional distress by subtracting patient self-ratings of emotional distress from spouse/friend observed ratings on parallel versions of the Ketterer Stress Symptom Frequency Checklist (KSSFC) [17]. In addition, Denollet [46,47] has found that social inhibition combined with emotional distress is a strong predictor of cardiac outcomes.

The present study was intended as a pilot investigation of the confounding/ independence of various proven psychometric predictors of mortality in ICHD populations as correlates of age at initial diagnosis.

Methods

Subjects

Subjects consisted of 83 patients (no. of females = 35, 42%) referred for stress management with a history of either positive catheterization (50% or greater luminal blockage of at least one of the proximal segments of the major epicardial arteries, or any occlusion of the left main segment) or a history of documented myocardial infarction. Mean age of the sample was: 56.7 (SD = 11.8). Mean age at initial diagnosis was: 52.3 (SD = 12.3).

For a subgroup of this sample, Spouse/Friend KSSFCs were received ($n = 58$ or 70%, No. of females = 21, mean age = 58.4, mean age at initial diagnosis = 54.0). Those subjects for whom a Spouse/Friend KSSFC was not received had: fewer years of education (12.5 vs. 13.8 years, $P = 0.016$); higher scores on the Beck Depression Inventory ($M = 26.0$ versus 13.8, $P = 0.048$); disproportionately fewer females (57% of females returned Spouse/Friend KSSFCs versus 77% of males, $P = 0.05$); and were more likely to be unmarried (48% of unmarried subjects failed to return Spouse/Friend KSSFCs versus only 23% of those who were married, $P = 0.03$).

Instruments

Psychometric instruments employed in the present study included the Beck Depression Inventory [48]; Crown-Crisp Phobic Anxiety Scale [49]; Ketterer Stress Symptom Frequency Checklist [50]; and Type D Scale [47]. The validity and reliability of these instruments are discussed elsewhere. Because the KSSFC has been found to be a superior predictor of death in a CAD sample [17], and we wanted to

minimize participant burden, we opted not to use the Cook-Medley Hostility Scale.

Procedures

At initial evaluation for enrollment in stress management, patients underwent a psychosocial history, mental status evaluation and completed the psychometric instruments noted above. Traditional cardiovascular risk factors were quantified by interview: Packyears of Smoking (maximum number of packs per day times the number of years a smoker); History of Diabetes; Body Mass Index; Snoring (as a proxy for sleep apnea); Sex; Marital Status (married versus divorced, widowed or single); History of Divorce (at least one versus none); History of Myocardial Infarction (MI) (at least one versus none); History of Revascularization (at least one percutaneous transluminal coronary angioplasty or coronary artery bypass surgery versus none); Early Family History of ICHD (at least one first or second degree relative having CHD prior to age 56 versus none); Current Smoker; History of Hypercholesterolaemia (max reading of 240 mg% or greater or currently treated); and History of Hypertension (highest casual blood pressures of 140/90 or greater or treated). They were then asked to have 'someone who knows you well' complete and return the Spouse/Friend Version of the KSSFC in a stamped and addressed envelope. Written instructions to the spouse/friend instructed them to complete and return the questionnaire before discussing it with the patient. Fifty-eight Spouse/Friend KSSFCs were received.

Analysis

The $P < 0.05$. level of significance was used.

The inter-relationship (and thus confounding/independence) of the psychometric measures was examined by running a correlation matrix for the continuous variables, and t -tests for the Type D Scale.

Univariate analyses (t -tests and Pearson product-moment correlation coefficients) were run between the psychometric measures and traditional risk factors, and age at initial diagnosis.

For only the psychometric measures, a Stepwise Multiple Regression was run to see if any of the psychosocial factors retained predictive value once the first was entered.

For the subgroup of subjects for whom Spouse/Friend KSSFCs were received, the same univariate and multivariate tests were rerun.

Results

The correlation matrix, and *t*-test for the Type D classification, revealed that almost all the scales were moderately to strongly related to one another. Only the Crown–Crisp Phobic Anxiety Scale was somewhat independent of some of the other scales, but still significantly associated with self-reported Depression and Anxiety on the Ketterer Stress Symptom Frequency Checklist as well as the Beck Depression Inventory (Table 2).

The univariate tests (*t*-tests and correlation coefficients) yielded statistically significant associations of age at initial diagnosis with Packyears of Smoking, Body Mass Index, History of MI and Early Family History of ICHD for both the total sample and Spouse/Friend KSSFC subgroup. For the total sample only, History of Hypertension was also significant. While Body Mass Index (larger), History of MI (positive) and Early Family History (positive) were all related to early diagnosis as would be expected, more Packyears of Smoking and a History of Hypertension yielded counterhypothetical results – a later age at initial

diagnosis. For the whole sample, self-reported AIAI ('aggravation, irritation, anger and impatience') and depression were associated with age at initial diagnosis. Despite the reduced sample size, and thus statistical power, in the Spouse/Friend subgroup, all three scales of the self-report KSSFC and the AIAI and Anxiety/Worry scales of the Spouse/Friend KSSFC were associated with age at initial diagnosis (Table 3). To examine the size of the effect, we divided the Spouse/Friend subgroup into two, based on the sample mean of the KSSFC AIAI Scale (*M* = 4.69, *SD* = 4.26). The mean age at initial diagnosis for those above versus below the sample was: 50.3 versus 56.8 years.

The stepwise multiple regression of the psychometric measures, for both the total sample and the Spouse/Friend KSSFC subgroup, both yielded only one significant predictor with all others losing significance once the first was controlled. Both regressions yielded an AIAI scale of the KSSFC; self-report in the total sample and spouse/friend report in the subgroup as the sole surviving predictor of age at initial diagnosis (Table 4).

Table 2 The association of various measures of emotional distress in the subgroup of patients referred for treatment of emotional distress, and for whom the Spouse/Friend Ketterer Stress Symptom Frequency Checklist (KSSFC) was available (n = 58)

	KSSFC							
	Patient			Spouse/Friend				
	AIAI	Dep	Anx	AIAI	Dep	Anx	BDI	CCPAS
KSSFC – Patient								
AIAI:		0.763	0.741	0.537	0.436	0.340	0.580	NS
Depression:			0.760	0.301	0.438	0.367	0.648	0.273
Anxiety:				0.269	0.363	0.395	0.530	0.318
Spouse/Friend								
AIAI:					0.540	0.644	0.378	NS
Depression:						0.755	0.376	NS
Anxiety							0.363	NS
Beck Depression Inventory								0.282
Note: NS=nonsignificant								
PLE ≤ 0.05=r of 0.219								
PLE ≤ 0.01=r of 0.306								
PLE ≤ 0.005=r of 0.337								
PLE ≤ 0.0005=r of 0.422								
(one-tailed, df=56)								
<i>t</i> -tests	Type D	Nontype D						
Patient	M	M	<i>P</i>					
AIAI	7.22	3.28	<0.001*					
Depression	6.67	3.43	<0.001*					
Anxiety	12.56	6.80	0.001*					
Spouse/Friend								
AIAI	6.72	3.78	0.013*					
Depression	4.89	2.83	0.003*					
Anxiety	11.00	5.25	0.002*					
Beck Depression Inventory	20.61	10.80	<0.001*					
Crown–Crisp Phobic Anxiety Scale	5.56	4.68	0.369					
	<i>n</i> =18	<i>n</i> =40						

AIAI, 'aggravation, irritation, anger and impatience'; BDI, Beck Depression Inventory; CCPAS, Crown–Crisp Phobic Anxiety Scale.

Table 3 **Traditional and psychosocial risk factors as univariate correlates of age at initial diagnosis in a sample of patients with known ischaemic coronary heart disease (ICHD)**

	Total sample (<i>n</i> = 83)		Spouse/friend subgroup (<i>n</i> = 58)	
	<i>r/t</i>	<i>P</i>	<i>r/t</i>	<i>P</i>
Traditional risk factors				
Pearson Correlations				
Packyears of smoking:	0.240	0.014*	0.316	0.008*
History of Diabetes:	0.156	0.080	0.096	0.237
Body Mass Index:	−0.231	0.018*	−0.274	0.019*
Snoring:	−0.068	0.271	−0.056	0.338
Years of education:	0.058	0.301	−0.041	0.381
Current age:	0.851	<0.001	0.863	<0.001
<i>t</i> -tests				
Sex:	−1.47	0.146	−1.18	0.242
Marital status:	−1.34	0.183	−0.63	0.528
History of divorce:	−0.21	0.834	−0.47	0.642
History of MI:	−2.77	0.007*	−2.46	0.017*
History of revascularization:	0.24	0.810	−0.02	0.983
Early family history of CHD:	2.65	0.010*	2.70	0.009*
Current smoker:	1.90	0.061	1.67	0.100
History of hypercholesterolaemia:	0.28	0.778	0.27	0.788
History of hypertension:	−2.04	0.044*	−1.52	0.133
Psychosocial risk factors				
Pearson Correlations				
KSSFC – Patient				
AIAI:	−0.265	0.008*	−0.303	0.010*
Depression:	−0.191	0.042*	−0.247	0.031*
Anxiety/Worry:	−0.158	0.076	−0.229	0.042*
KSSFC–Spouse/Friend				
AIAI:	NA		−0.336	0.005*
Depression:	NA		−0.119	0.187
Anxiety/Worry:	NA		−0.289	0.014*
Beck Depression Inventory:	−0.023	0.417	−0.056	0.339
Crown–Crisp Phobic Anxiety Scale:	−0.009	0.469	−0.043	0.375
<i>t</i> -tests				
Type D:	−1.49	0.139	−1.50	0.140

KSSFC, Ketterer Stress Symptom Frequency Checklist; AIAI, 'aggravation, irritation, anger and impatience'.

Table 4 **Results (*P* values) of univariate and multiple regression determining unique psychometric predictors of age at initial diagnosis in a sample of patients with known CAD (*n* = 83) and a subset for whom Spouse/Friend KSSFC is available (*n* = 58)**

	Total sample		Spouse/friend subgroup	
	Univariate	Stepwise	Univariate	Stepwise
KSSFC–Patient				
AIAI	0.008*	0.016*	0.010*	0.253
Depression	0.042*	0.962	0.031*	0.228
Anxiety	0.076	0.511	0.042*	0.258
KSSFC–Spouse/Friend				
AIAI	NA		0.005*	0.010*
Depression	NA		0.187	0.557
Anxiety	NA		0.014*	0.457
Beck Depression Inventory	0.417	0.717	0.339	0.545
Crown–Crisp Phobic Anxiety Index	0.469	0.880	0.375	0.683
Type D Scale	0.139	0.679	0.140	0.466
		<i>F</i> = 6.09 <i>df</i> = 1,81 <i>R</i> ² = 0.070		<i>F</i> = 7.14 <i>df</i> = 1,56 <i>R</i> ² = 0.113

KSSFC, Ketterer Stress Symptom Frequency Checklist; AIAI, 'aggravation, irritation, anger and impatience'.

Discussion

Clinical care of psychosocial/emotional distress in ICHD populations is almost wholly neglected, despite

compelling evidence of reduced chest pain [25–28], reduced ischaemia [25,51], greater compliance [52,53] and reduced death and MI rates in response to

treatment [29]. One barrier to accomplishing such care is the absence of a brief, and validated, screening tool(s) for identifying patients at risk for the various adverse outcomes. In prospective studies, multiple psychometric questionnaires have been found to have strong predictive power. However, the extent to which these instruments are redundant, or independent, in predicting clinical outcomes remains unclear. The present study was intended as a pilot investigation into this question, using age at initial diagnosis, as a cross-sectional proxy for likely disease malignancy.

The limitations of the present investigation include the nature of the sample (patients referred for stress management), which may have skewed the results in unpredictable ways. Given the average scores observed in this sample, it is clear that this is a highly distressed sample. This result might be expected to constrain natural variability in the sample, and thus weaken any of the observed associations. Additionally, patients for whom the first sign of ICHD was sudden death or those who were not identified by referring physicians as 'stressed' would not be included here. Totally asymptomatic patients would also have been unavoidably excluded. It is impossible to know whether these sampling biases would have strengthened or weakened the observed relationships. For example, if the relationships observed here, and in multiple prospective studies [18], are real, then those patients dying young and without prior diagnosis would be expected to be the most extreme cases. Given that they are not included in this sample, a conservative bias exists. A non-clinically selected sample recruited from a source of patients with known ICHD status (e.g., patients with coronary artery disease by catheterization) would be needed to minimize/avoid these potential biases.

Another consideration is the very strong association of current age and age at initial diagnosis. The most simple explanation of this effect is that patients who are diagnosed earlier are also likely to be referred for stress management earlier. However, the possibility of a cohort effect might be entertained; perhaps younger people are intrinsically more distressed regardless of disease status? In fact, in cross-sectional epidemiological studies, the rate of depression and some anxiety disorders is higher in younger age groups [54]. This is generally attributed to a higher death rate among emotionally distressed subjects [55,56] because of more suicides; increased accidents; greater nicotine, alcohol and drug usage [57,58]; noncompliance to chronic preventive medical regimens [52,59,60]; and

diminished immunocompetence [61,62] or greater sympathoadrenomedullary arousal [63]. Thus, we believe the strong association of current age and age at initial diagnosis (AID) is an artifact of earlier referral.

We observed a strong propensity for multiple measures of emotional distress to be intercorrelated, raising questions about whether only one (or a few) are necessary in clinical settings to identify at-risk patients. The redundancy of the psychometric measures in predicting age at initial diagnosis in the multiple regressions confirms this belief, and replicates our previous study [64]. Once one validated measure is used, the others seem to lose any utility as correlates of age at initial diagnosis. This finding needs to be replicated in a prospective fashion for all important clinical outcomes (i.e., emotional distress, chest pain, disability, non-fatal MI, death and, arguably, health system utilization) before firm screening recommendations can be made.

We believe it important that a measure of anger/hostility emerges from both of our multiple regressions as the single unique and most potent predictor variable. This finding replicates our results from a previous sample [64], and implies that anger/hostility may be the earliest phase of stress for many patients developing early heart disease [65–67].

Body Mass Index, History of MI and Early Family History of coronary heart disease were related to age at initial diagnosis as might be expected. The fact that Packyears of Smoking and History of Hypertension are counter-hypothetically related to early diagnosis also replicates our previous results [64]. While the selection biases operative in our sample may account for this, it is also possible that within a sample selected to have known coronary artery disease, a strong smoking history and hypertension may only predict later onset ICHD. Such a finding might account for the loss of predictive power commonly observed in prospective studies for these factors in diagnosed, as opposed to initially healthy, samples [1–3]. Again, prospective data must settle this issue.

Present results need replication in a single-sample, prospective risk factor study using all-important clinical endpoints. Ideally such a study would be large enough to examine the sexes separately since males and females may differ in acknowledging emotional distress [68]. However until such a dataset becomes available, we believe clinicians are justified in using any

of the prospectively-validated, unique psychometric scales with the strongest risk ratios [18] for screening purposes. Some of these instruments are brief, and easily scored and could therefore be used to provide immediate feedback for patient–doctor discussion (e.g., the Beck Depression Inventory or the Crown–Crisp Phobic Anxiety Scale), while others require more complex scoring algorithms (e.g., the Ketterer Stress Symptom Frequency Checklist or the Type D Scale) necessitating a delay in availability of results to clinicians. The content of some scales (e.g., sexual or suicidal items) may make some instruments less acceptable to patients or physicians (e.g., the Beck Depression Inventory).

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